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Behavioral Effects of Exposure to Solvent Vapors

Experimental and field studies

by
Francesco Gamberale

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From the Work Physiology and Work Psychology Divisions
Department of Occupational Medicine
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BEHAVIORAL EFFECTS OF EXPOSURE TO SOLVENT VAPORS

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BIBL.

The following studies are summarized and discussed in this paper:

(1) Gamberale, F. and Hultengren, M. Toluene exposure: II. Psychophysiological functions. Work-environ.-health 9 (1972) 131-139

(2) Gamberale, F. and Hultengren, M. Methylchloroform exposure: II. Psychophysiological functions. Work-environ.-health 10 (1973) 82-92

(3) Gamberale, F. and Hultengren, M. Exposure to styrene: II. Psychological functions. Work-environ.-health 11 (1974) 86-93

(4) Gamberale, F., Annwall, G. and Hultengren, M. Exposure to white spirit: II. Psychological functions. Scand. j. work. environ. & health 1 (1975) 31-39

(5) Gamberale, F., Annwall, G. and Hultengren, M. Exposure to methylene chloride: II. Psychological functions. Scand. j. work environ. & health 2 (1975) 95-103

(6) Gamberale, F. and Svensson, G. The effect of anesthetic gases on the psychomotor and perceptual functions of anesthetic nurses. Work-environ.-health 11 (1974) 108-113

(7) Gamberale, F., Lisper, H.O. and Anshelm-Olson, B. Styrengasers effekt på reaktionsförmåga hos arbetare i plastbåtsindustri. Arbete och Hälsa 8 (1975) 1-23

(8) Gamberale, F. Behavioral toxicology: a new field of job health research. AMBIO 1 (1975) 43-46

Reference to the investigations will be made using the arabic numerals given above.

C O N T E N T S

	Page
INTRODUCTION	7
METHODS	10
Experimental design and procedure	10
Behavioral performance tasks	13
EFFECTS OF EXPERIMENTAL EXPOSURE	15
Background	15
Concentration of solvents in alveolar air and arterial blood	15
Behavioral performance changes during exposure	16
Subjective reactions to exposure	20
Heart rate during exposure	21
EFFECTS OF OCCUPATIONAL EXPOSURE	22
Background	22
Results of field studies	23
CONCLUDING REMARKS	26
ACKNOWLEDGEMENTS	27
REFERENCES	28

INTRODUCTION

Classical toxicological criteria based on obvious injury assessed with clinical, epidemiological or experimental studies have too often been found inadequate, in view of the increasing demands for prevention of health hazards from chemicals. Indeed, the classical toxicological approach based on lethality and advanced pathology implies an arbitrary safety factor (Barnes & Denz 1954). The kind of exposure to chemical agents occurring most commonly in the occupational environment, i.e., exposure to relatively low doses, only rarely causes specific, definite pathological symptoms. However, the results of several investigations (8; see also text on pp. 15, 22) clearly show that exposure to a number of substances commonly found in the occupational environment often causes impairment to the nervous system's functional capacity. For this reason, toxicology is now taking an increasing interest in biological and behavioral tests and procedures suitable for a quantitative evaluation of the effects of exposure to chemical substances also at low dose levels. The major objective of this developmental trend in modern industrial toxicology is to find ways to detect, at the earliest possible moment in biological time, changes of systemic or of nuisance nature that may be affecting workers.

Because of their widespread use in most occupations and industries, a very serious threat to the health and efficiency of workers comes from industrial solvents.

The term industrial solvent generally refers to those organic liquids which dissolve many water-insoluble products such as fats, waxes, resins etc, forming a homogeneous solution. An important property of industrial solvents is that the solute can be recovered with its original properties intact when the solvent is removed from the solution. Due to these properties, solvents have come to be used extensively in industry. Different forms of surface coating are made possible by solvents, such as printing inks, glues, paints and spreading preparations for paper and fabrics of various types. Solvents are used to reduce materials to a plastic condition so that they can be moulded, extruded or otherwise shaped.

They are used in the processes of extracting oils, fats and other substances from different products.

The uptake in the organism of industrial organic solvents takes place principally through inhalation of the vapor. The solvent vapor inhaled diffuses from the alveoli to arterial blood, from which it diffuses to the tissues. The same mechanism of diffusion accounts for the elimination of most of the solvent from the organism. Diffused from the tissues to venous blood, the solvent reaches the lungs and is expired. (For a detailed description of the uptake of solvents in the organism see Åstrand 1975.) A determinant factor for the uptake of solvents in the tissues of the nervous system is the solubility of the solvent in fat. The nerve cells, because of their content of fatty substances, are especially sensitive to solvents circulating in the blood and there is evidence indicating that the solubility in fat is directly related to the neurotoxicity of the solvents (Lowe & Hagler 1969).

The health hazards arising from exposure to solvents are due to the toxic action of these substances on the organism. Apart from causing dermatitis, damage to the liver and other specific effects, all organic solvents affect the central nervous system, acting as depressants and anesthetics. Depending upon the degree of exposure, these effects may range from mild subclinical manifestation to narcosis and death from respiratory arrest. Between these extremes there is a whole spectrum of effects (see Gerarde 1969; Browning 1965).

The reaction of an individual to a solvent will be affected by the specific toxicity of the solvent itself, and by the duration and extent of exposure. To give guidance concerning the extent to which atmospheric contamination in the working environment should be limited, figures indicating the threshold limit value (TLV) are produced for different substances, including solvents. The TLVs represent "conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect" (American Conference of Governmental Industrial Hygienists 1974). Thus, the TLVs allow for the possibility of genuine, but trivial, effects, or even for the development of occupational illness in a small percentage of the exposed workers. The setting of a TLV is based on available information from industrial experience and from experimental studies on humans and animals. The TLVs for solvents are set not only to prevent acute effects but also

to prevent the occurrence of chronic manifestations (Arbetarskydds-styrelsens anvisningar 1974).

The general purpose of the studies referred to in the present paper was to investigate the functional effects of acute exposure to industrial solvents. The investigations were motivated by the need for prediction of health hazards from industrial solvents at concentrations commonly found in the occupational environment. The outcome of the investigations was intended as a possible contribution to knowledge of the effects of exposure to solvents, which is the basis for the development of TLV.

Generally speaking, all physiological and behavioral measures are functional measures. In the present context the term functional refers to those measures which reflect activity of the central nervous system. They are generally measures of performance or factors associated with performance. The measurement of performance is accomplished by providing the individual with a task and recording quantities such as errors, speed, or the time needed to reach a criterion level of achievement. The performance measures depend upon behavioral and physiological processes, i.e. processes in the central nervous system, which are conditioned by variables associated with the task and, most important, by the environmental conditions.

During the last decades performance has been studied intensively under numerous task and environmental conditions, and large quantities of data have been accumulated. In spite of this, no general behavioral or psychophysiological theory is available which embraces the effects of environmental conditions on human performance. Nor are there any satisfactory criteria to evaluate which impairments in performance should be regarded as dangerous and which should not. In the present investigations interest was simply focused on the occurrence of an effect at levels of exposure which have practical importance, i.e., at levels around the TLV.

The investigations summarized in the present paper were promoted by the arbitrary, but in our opinion reasonable assumption, that results showing an exposure level of an agent to be capable of affecting the functional capacity of the nervous system of humans provide valuable information, not least in the evaluation of the TLV for the agent. The occurrence of such effects in the work environment may indeed constitute an occupational problem in different ways. The efficiency of exposed

workers may be reduced if their jobs entail special demands on human performance capabilities. Exposure may make the workers more accident-prone on and off the job. Also, perhaps more important, behavioral effects may be early warning signs of physiological impairment to the central nervous system, which, in chronically exposed workers, may develop into permanent damage.

Five of the investigations referred to in this paper (Studies 1 to 5) were experimental laboratory studies on human subjects exposed to the industrial solvents toluene, methylchloroform, styrene, white spirit and methylene chloride respectively. The investigations were conducted at the Work Physiology Division, Department of Occupational Medicine, National Board of Occupational Safety and Health, Stockholm. They were part of a research project also including the study of the uptake of the solvents in the human organism (Åstrand et al 1972, 1973, 1974, 1975a, 1975b). Two of the investigations were field studies, concerned with the possible effects on performance of occupational exposure to anesthetic gases such as halothane and nitrous oxide (Study 6) and to the industrial solvent styrene (Study 7).

METHODS

Experimental design and procedure

The experimental laboratory investigations (Studies 1 to 5) were carried out with healthy male subjects, either employees of the Department of Occupational Medicine or university students partaking as paid volunteers. The investigations were performed with strict adherence to the ethical and technical requirements for human inhalation experiments, which included the informed consent of each subject after the objectives of the study and the nature of the procedure had been explained. However, the subjects were not informed about the order of conditions.

A group of 12 - 14 subjects participated in each investigation. They carried out the performance tasks during each of four successive periods of exposure to concentrations of solvent vapor as indicated in Fig 1. Each exposure period lasted 20 - 30 minutes. In Studies 1 and 2 the

subjects were given a five minute rest from exposure between the second and third exposure periods. In Studies 3 to 5 there was no interruption of exposure. The same subjects were also studied under control conditions with exposure to atmospheric air, in which all operations and measurements were the same as during exposure to the solvents. The control session was performed for each subject at the same time of day as the experimental session. The interval between the two sessions was 7 days. Every other subject was studied during the experimental condition first, and every other during the control condition first. Study 4 also comprised a series of trials with subjects exposed to 4 000 mg/m^3 in inspiratory air for 50 minutes and to control conditions.

Human experimental exposure to gases or solvent vapor is usually carried out in controlled-environment chambers, in which exposure and other environmental factors can be controlled and varied. However, in Studies 1 to 5, as well as in the physiological part of the investigations, the solvent vapor was administered with a relatively unusual technique which was found to be more suited to the experimental design adopted. The inspiratory air and solvent vapor mixture was administered through a tube via a breathing valve and a mouthpiece with very low breathing resistance (Kilbom 1971). This technique made a quick change of exposure level possible and facilitated the procedure of taking samples of inspired and alveolar air during the tasks. Furthermore, the subject's eyes and nose could be spared from exposure, with consequently less risk of local irritation. However, the use of a mouthpiece and nose clip was a limiting factor with regard to the possible duration of the experimental exposure.

The concentration of solvents in inspiratory air was continuously monitored with a hydrocarbon analyser (for more details and for the preparation of the solvent vapor standards see Åstrand et al 1972, 1973, 1974, 1975a, 1975b).

As a measure of the biological level of exposure during the experiments, alveolar air samples were intermittently collected for each subject. The measurement of the concentration of solvents in alveolar air was used, when possible, to estimate the concentration of the solvents in arterial blood. Such estimation was made possible by the study of the relation between the two variables. This was performed on separate occasions by exposing one or two subjects to the same exposure levels

as used during the experiments, and collecting parallel samples of alveolar air and arterial blood.

In experimental investigations of the type referred to in this paper, changes in performance may occur which are not due to the experimental variables under investigation and which may systematically affect the direction of the differences found in the experiments. A number of possible confounding factors were, however, considered in the planning and conduction of the investigations. They were dealt with using customary operations of experimental control. Special attention was paid to the problem of possible effects on performance arising from the subjects becoming aware of the condition of exposure (see Frankenhauser et al 1963). In order to avoid or limit this potential problem, the presence or absence of the solvents was disguised for subjects by introducing a receptacle containing menthol crystals into the tube leading to the breathing valve in both experimental and control conditions.

In Studies 3 and 4 additional measures were found necessary in order to attain the most identical perception of conditions possible by subjects. Thus the subjects had to continue breathing through the mouthpiece for a few minutes after termination of exposure. Moreover, control conditions were started and terminated with a smell of solvent in the mouthpiece, which was comparable to that of the experimental conditions.

In order to assess whether or not the subjects had been able to distinguish exposure to solvent from exposure to air, each subject was asked a few standardized questions after completion of exposure on the second day of trials. Furthermore, immediately before the termination of exposure on both days of trials, subjects were asked to evaluate their own condition with respect to the following six variables: calm - hurried, active - passive, relaxed - tense, well disposed - indisposed, affected - unaffected and alert - tired. Assessments were facilitated with the aid of 7-point scales in which extreme values were defined by opposites, and the scale value 4 corresponded to the "normal" state for the individual. As an additional measure of control of possible emotional changes occurring during the trials, the subjects' heart rate was recorded intermittently during both conditions, using telemetric equipment (Medenik Honeywell).

The evaluation of the magnitude of exposure constitutes a special problem in field investigations. The monitoring of the breathing zone of the subjects will provide adequate measures of exposure only in those rare environmental conditions which are stable and unchanged. When the concentration of solvents fluctuates in the work areas, the measurement of exposure will require continuous monitoring of the breathing zone. Even when this is done during the period of investigation (as in Studies 6 and 7), the validity of the measurements, i.e., the extent to which the measurements reflect the "true" situation, will be difficult to establish. Furthermore, the exposure data collected will of course not yield information as to the past, and will therefore not be applicable in the study of long term exposure.

The effects of long term exposure to neurotoxic substances, including industrial vapor solvents, on the central nervous system can hypothetically range from slight functional changes of short duration which disappear immediately after the cessation of exposure, to irreversible brain disfunctions. Since only a few investigations have as yet been conducted on the effects of occupational exposure on behavioral performance, Studies 6 and 7 could not be based on any specific hypothesis as to the nature of the effects to be expected. The investigations were therefore designed in such a way that, within the limits of a non-longitudinal study, some information could be gained about the possible duration of an observed effect. In both investigations, measurements of psychomotor performance were made at the beginning and at the end of a working day, using both an exposed and an unexposed group. All the measurements were carried out in conjunction with the subjects' natural work routines.

In Study 6 the experimental group consisted of anesthetic nurses who were exposed to low doses of anesthetic gases in their daily work. Unexposed nurses with varying intensive care duties constituted the control group. The experimental group of Study 7 comprised workers from four plastic boat industries who were exposed daily to styrene. The control group consisted of workers from two mechanical industries.

The behavioral performance tasks

The behavioral performance tasks used to assess changes in the central nervous system caused by chemical substances are many and varied. It is

necessary only to look at the literature concerning the effects of alcohol or carbon monoxide to come up with an impressive list of different tasks and task devices aimed at the measurement of behavioral performance. The question of which tasks or which performance functions are more sensitive to exposure has not yet been answered for a single substance. The greatest obstacle to the assessment of the differential impairment of mental functions is constituted by the difficulty in attributing a measured performance impairment to a specific process in a test situation, which always involves sensory as well as central and response processes. Probably the only direct attempt to study differential impairment in exposure to industrial solvents was accomplished by Winneke et al (1973), using dichloromethane and large batteries of functional tests. The inhalation of 0.03 to 0.08 Vol % of the solvent resulted in a pattern of generalized impairment of psychomotor performance and vigilance behavior, while no performance impairment was observed in the cognitive tasks used, i.e., tasks of learning performance and visual organisation. In spite of the difficulty in generalizing results, there seems to be a general tendency among researchers to assume that cognitive functions are more resistant to chemical agents than psychomotor or perceptual functions. Results from studies on the effects of alcohol (Myrsten 1971; Goldberg & Myrsten 1974) and of carbon monoxide (for reviews see U.S. Dept of H.E.W., NIOSH 1972; U.S. Dept of H.E.E. 1970) seem to support this assumption.

With the exception of a task of short term memory and one of mental arithmetic used in Studies 4 and 5, all the behavioral performance tasks chosen for our investigations were of the psychomotor and perceptual type. They consisted of tasks of simple and choice reaction time, perceptual and sensory-motor speed and manual dexterity and coordination. The cognitive tasks introduced in the test battery of Studies 4 and 5 were performed with the aid of electronic instruments and a display-control panel. Each task could be performed in a few minutes (3 to 6 min) and required a minimum of instructions. All the tasks were such as to facilitate an analysis of the subjects' performance over time.

EFFECTS OF EXPERIMENTAL EXPOSURE

Background

Previous to the present investigations, only few experimental laboratory studies had been accomplished to investigate the effects of vapor solvent on human performance capability (Stopp & McLaughlin 1967; Winneke et al 1968, 1973; Vernon & Ferguson 1969; Schlipköter et al 1970; Salvini et al 1971a, 1971b; Di Vincenzo et al 1972). None of these studies were systematic, in the sense that more than one solvent or more than one concentration of a solvent was studied with the same experimental technique and tasks. Thus, previous investigations did not yield any consistent knowledge concerning the level or duration of exposure at which the investigated solvents can be expected to produce effects on performance. The importance of using more than one concentration in order to establish a dose-response relationship has recently been discussed by Stewart et al (1974) in their critical evaluation of previous studies.

Concentration of solvents in alveolar air and arterial blood

The concentration of a solvent in arterial blood depends primarily on the amount of solvent entering the alveoli, on the solubility of the gas in blood and on the rate of the blood circulation (Åstrand 1975). In Studies 1 to 5, alveolar air samples were taken intermittently during the experimental sessions. For all solvents, the concentration in alveolar air rose sharply during the first 5 - 10 min of each exposure period, rising thereafter only slightly throughout the rest of the period. The arterial blood concentration was found to be a very close linear function of the alveolar air concentration in the case of toluene (Study 1), methylchloroform (Study 2), aliphatic components of white spirit (Study 4) and methylene chloride (Study 5). With regard to styrene (Study 3) and aromatic components of white spirit (Study 4), the concentration in arterial blood rose continuously during each exposure period and a poor and non-linear relationship with alveolar air concentration was obtained (Åstrand et al 1974, 1975a). Thus, with the exception of styrene and aromatic components of white spirit, the concentration of the solvents in arterial blood during experimental exposure could be estimated fairly accurately from the concentration in alveolar air. Styrene, contrary to

the other solvents investigated, is highly soluble in blood. This quality of the solvent was probably most responsible for the poor correlation obtained between the concentration in alveolar air and in arterial blood. The relationship between the concentration of a solvent in alveolar air and arterial blood was recently postulated by Åstrand (1975) to be affected by the solubility of the solvent in blood. Generally, it can be stated that solvents with high solubility in blood will reveal poor correlations between the concentration in alveolar air and in arterial blood. On the other hand, the correlation between the two measures can be high for solvents with low solubility in blood.

Another variable of special importance in the evaluation of the uptake of a solvent in blood is pulmonary ventilation. With increased pulmonary ventilation, as in physical work, the amount of solvent taken up by the blood is greater than during rest (see Åstrand et al 1972, 1973, 1974, 1975a, 1975b). In the physiological investigations concerned with the uptake of the solvents in the organism (see reference above), subjects reached a concentration in arterial blood, which, depending on the type of solvent inspired, was about 1.4 to 3.6 times greater when working on a bicycle ergometer at 50 W for 30 min than at rest during the psychological trials at an exposure to the same concentration in inspiratory air. In terms of the load in respiratory and circulatory organs, a work intensity of 50 W corresponds to those encountered in many occupations in which there is exposure to solvents (Åstrand 1971). The above-mentioned results concerning the effects of work on the uptake of solvents in the organism should be given serious consideration whenever evaluating the risk for the occurrence in real-life situations of an effect observed in an experimental setting, where the subjects are not physically exerted.

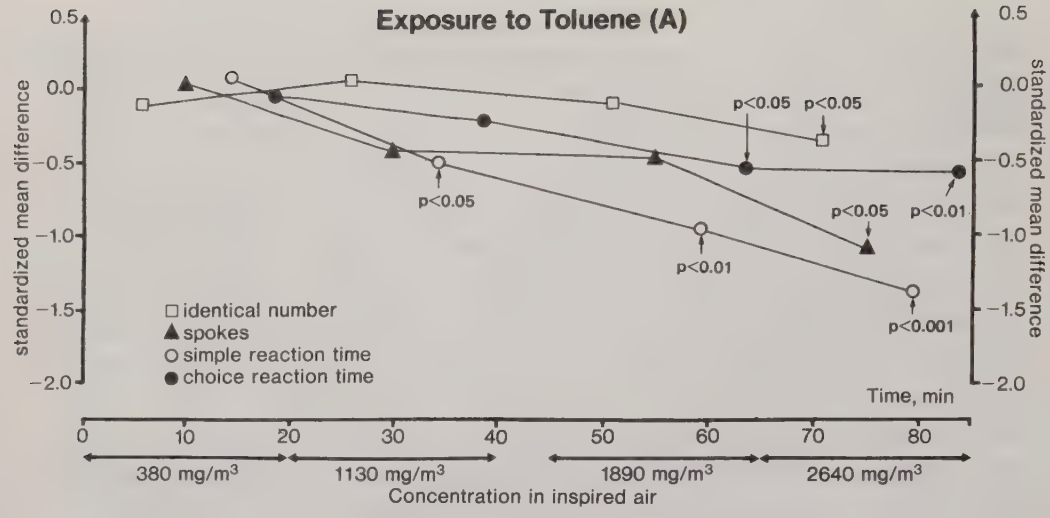
Behavioral performance changes during exposure

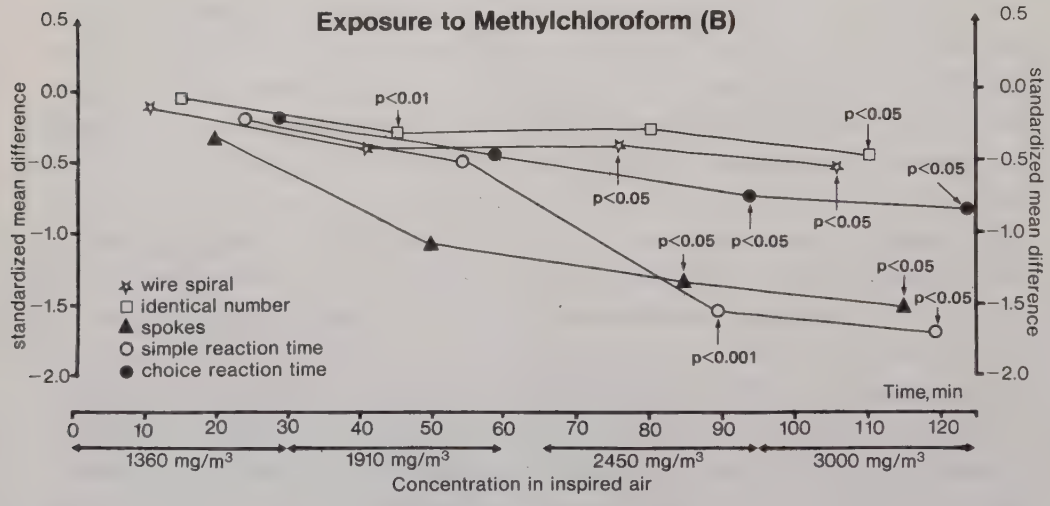
The main results regarding the effects on performance of exposure to the different solvents is illustrated in Fig 1, where standardized mean score differences between experimental and control conditions are related to the level and duration of exposure.

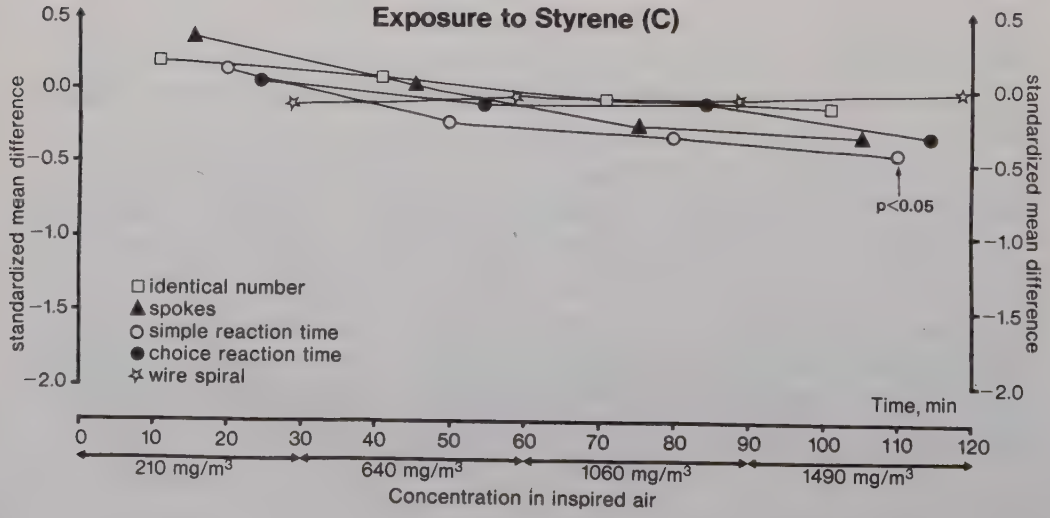
As can be seen in Fig 1, exposure to toluene (Diagram A) and methylchloroform (Diagram B) produced statistically significant impairment of subjects´ mean performance in all the tasks. Furthermore, the differences

in performance between experimental and control conditions clearly increase as a function of the level and duration of exposure to the solvents. Subjects' performance was also adversely affected by exposure to styrene (Diagram C). The effects of this solvent, however, were not as evident as for toluene and methylchloroform. Thus, performance during exposure to styrene was significantly impaired only in a task of simple reaction time ($p < 0.05$). No impairment in performance could be observed in exposure to white spirit in concentrations up to 2 500 mg/m^3 in inspiratory air (Diagram D), nor in exposure to methylene chloride in concentrations up to 3 470 mg/m^3 in inspiratory air (Diagram E). In the case of white spirit, for which no TLV was available, the negative results obtained led to a further series of trials with subjects exposed to a concentration of the solvent in inspiratory air of 4 000 mg/m^3 for 50 min. This concentration of the solvent was found to impair subjects' reaction time and probably also their short-term memory. Because of the metabolism of methylene chloride, resulting in carboxyhemoglobin (COHb), further investigations with higher concentrations of this solvent were not conducted since COHb would definitely have exceeded levels accepted in occupational exposure.

When interpreting the findings of this series of experimental investigations, the following circumstances should be noted. The adverse effects of the solvents on human performance capability were observed after relatively brief periods of exposure. Therefore, the results do not preclude the possibility that solvents may also affect man's psychophysiological efficiency at lower concentrations after exposure of longer duration. This possibility should be considered seriously, especially with regard to those solvents like styrene, which being highly soluble in blood and fat, are easily accumulated in the organism. Moreover, as already pointed out, the uptake of the solvents in the organism is greatly affected by physical activity. Since physical activity is a normal feature of most of the work sites at which exposure may occur, it logically follows that, in real work situations as compared to experimental conditions, the same concentration of a solvent in inspiratory air should result in higher uptake and thereby in greater risks for functional effects. According to the reasoning above, it can be stated that impairments in behavioral performance capability, i.e., impairment in the functioning of the central nervous system, were observed during exposure to toluene and methylchloroform at blood levels which are usually exceeded when workers are exposed to concentrations of the solvents approaching the TLVs.


Exposure to Toluene (A)
standardized mean difference
0.5
0.0
−0.5
−1.0
−1.5
−2.0
p<0.05
p<0.05
p<0.05
p<0.01
p<0.05
p<0.01
p<0.001
□ identical number
▲ spokes
○ simple reaction time
● choice reaction time
Time, min
0 10 20 30 40 50 60 70 80
380 mg/m³
1130 mg/m³
1890 mg/m³
2640 mg/m³
Concentration in inspired air


Exposure to Methylchloroform (B)
standardized mean difference
0.5
0.0
−0.5
−1.0
−1.5
−2.0
p<0.01
p<0.05
p<0.05
p<0.05
p<0.05
p<0.05
p<0.05
p<0.05
p<0.05
p<0.001
☆ wire spiral
□ identical number
▲ spokes
○ simple reaction time
● choice reaction time
Time, min
0 10 20 30 40 50 60 70 80 90 100 110 120
1360 mg/m³
1910 mg/m³
2450 mg/m³
3000 mg/m³
Concentration in inspired air


Exposure to Styrene (C)
standardized mean difference
0.5
0.0
−0.5
−1.0
−1.5
−2.0
p<0.05
□ identical number
▲ spokes
○ simple reaction time
● choice reaction time
☆ wire spiral
Time, min
0 10 20 30 40 50 60 70 80 90 100 110 120
210 mg/m³
640 mg/m³
1060 mg/m³
1490 mg/m³
Concentration in inspired air

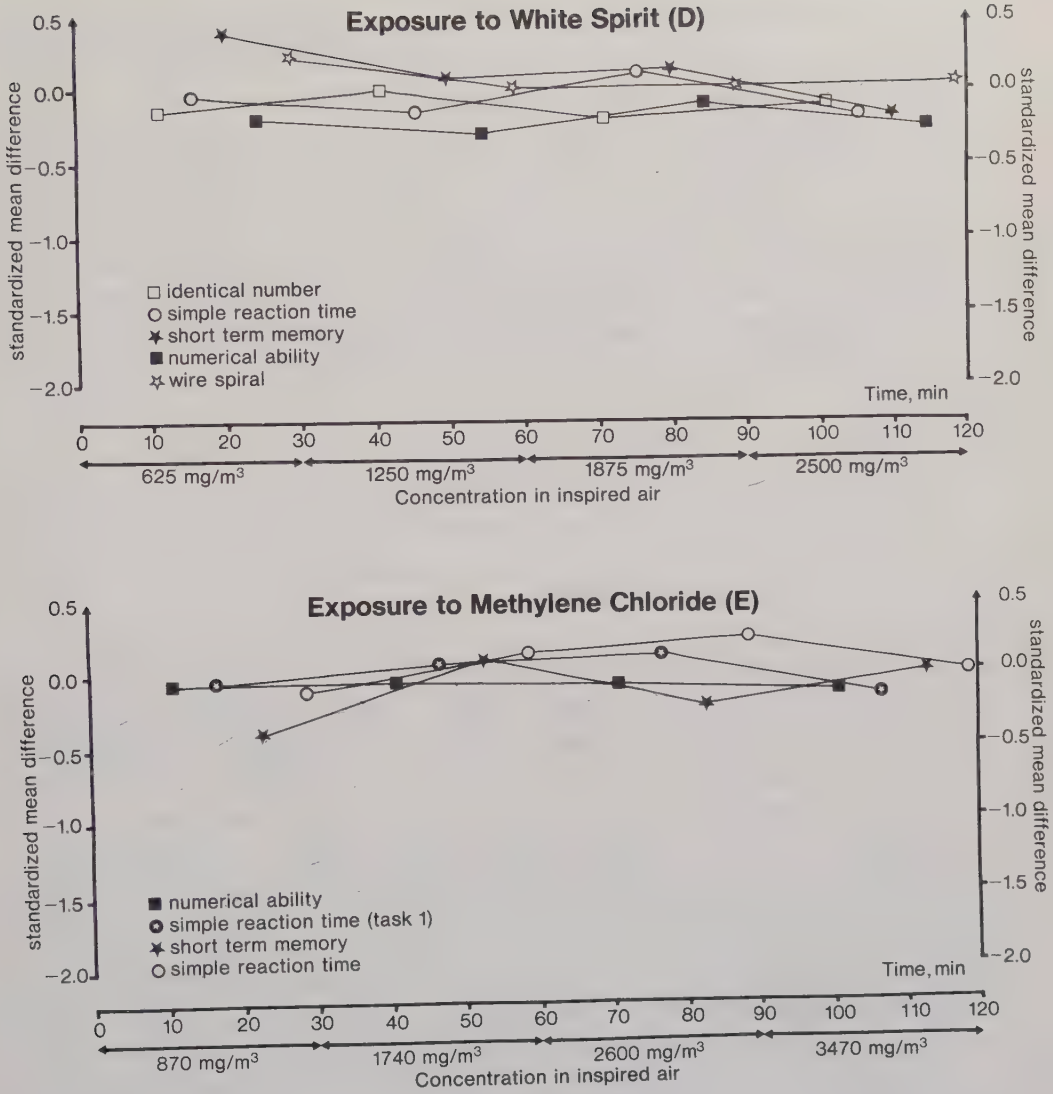


Fig 1 Standardized mean score differences between experimental and control conditions for different tasks as related to the level and duration of exposure to toluene (Diagram A), methylchloroform (Diagram B), styrene (Diagram C), white spirit (Diagram D) and methylene chloride (Diagram E). The standardized mean score differences were obtained by dividing each mean score difference between experimental and control conditions with the mean of standard deviations in control conditions. When necessary a sign has been reversed, so that any performance decrement in experimental condition as compared to control conditions is stated in the diagrams with a negative sign. The arrows in the diagrams indicate statistically significant intra-pair mean differences between conditions. (Adapted from 1, 2, 3, 4, 5.) At the time of the investigations the TLVs were: 750 mg/m^3 for toluene, 1 900 mg/m^3 for methylchloroform, 210 mg/m^3 for styrene and 1740 mg/m^3 for methylene chloride. No TLV was established for white spirit.

The experimental investigations described in the present paper were not designed to examine the differential sensitivity of functional tests to the action of solvent vapor. However, according to the results obtained, tests of reaction time, especially those of simple reaction time, appeared to give the most consistent results throughout the different experimental conditions studied. Thus, with the possible exception of methylene chloride, all the solvents investigated resulted in impaired performance on a task of simple reaction time. In view of this circumstance the results would appear to suggest that simple psychomotor functions are exposed to an earlier, more direct action by the solvent than more complex functions.

Subjective reactions to exposure

The results of the interviews following exposure to toluene (Study 1), methylchloroform (Study 2), white spirit (Study 4) and methylene chloride (Study 5) clearly revealed that subjects had been unable to distinguish between experimental and control conditions. Thus the action taken to disguise exposure had been effective with these solvents. With regard to styrene (Study 3), the interviews indicated that the subjects had been able to note certain differences between the conditions with and without exposure to the solvent. However, the local irritation which styrene usually produces was almost completely absent in this experimental exposure. This result was undoubtedly due to the special technique adopted which spared nose and eyes from exposure. The analysis of the results from the subjects' assessment of their condition after both trial days confirms the above conclusions that only exposure to styrene could be perceived as differing from control conditions. Thus the only differences between conditions for any of the assessment variables were found in Study 3, where subjects evaluated themselves as being more "tense" and "affected" in exposure to styrene than in exposure to air. The possibility of subjective reactions having exerted systematic effects on performance cannot as a matter of course be completely excluded in any of the studies performed. However, even in the case of styrene, the occurrence of such effects was considered improbable.

Heart rate during exposure

When an individual is placed in a situation which demands physical or mental effort, heart rate generally increases. Regarding mental effort, the mechanism and degree of the rate reaction are related to the individual´s conscious or unconscious evaluation of the situation, his prior experience and his previously established reaction pattern. In a situation which is new and interesting, heart rate may increase and, when the situation becomes known and routine, or when interest decreases, heart rate may fall (Deane 1966; Campos & Johnson 1966; Obrist 1963).

In Studies 1 to 5 heart rate was recorded at a given point during the performance of each task. The measurement of heart rate was primarily aimed to be a control of possible emotional changes, related to the subjects´ experience of conditions, which might affect performance.

The analysis of each subject´s heart rate reaction did not reveal any case of changes which could be attributed to subjective experience associated with exposure to solvent. The differences in heart rate between conditions were always very slight and within the range of chance differences.

In other respects, very consistent results were obtained throughout Studies 1 to 5. Thus, heart rate always declined between exposure periods as the performance tasks were repeated. This systematic decline in heart rate was due in all probability to the subjects´ increasing familiarity with the test situation and with the individual tasks. This interpretation is also supported by the fact that the individual values always proved to be lower during the second than during the first trial day. Heart rate was also found to be a function of the performance task during which it was recorded. This statement is based on the fact that the differences in heart rate between the tasks, while being relatively small, always displayed a similarity of mutual relationship on the different measurement occasions, such as could not be entirely ascribed to sequence effects.

According to the above results, there seems to be a level of heart rate specific for the performance requirements of a behavioral task. While this is of course the case for tasks requiring physical exertion, the results seem to be somewhat surprising in tasks of mental performance.

According to Kalsbeek (1971) "tasks obviously differing in many aspects, but falling largely within the mental work capacity cannot be expected to give rise to distinguishable physiological reactions" (page 107). The results obtained in the present investigations do not seem to be in accordance with the above statement. With regard to the nature of the differences found among tasks with respect to heart rate, the hypothesis is forwarded that heart rate is a function of the specific level of arousal exerted on the subjects by the tasks.

EFFECTS OF OCCUPATIONAL EXPOSURE

Background

While numerous case studies have shown examples of acute intoxication as well as of suspected or probable chronic intoxication caused by occupational exposure (see Browning 1965), the literature only comprises a few investigations of the epidemiological type, i.e., studies of populations of exposed workers. Some of these studies (Hänninen 1971; Götell et al 1972; Lindström 1973; Tolonen 1974; Blume et al 1975), have provided evidence of impaired behavioral performance capability in groups of exposed workers with no manifest symptoms of intoxication. Further evidence that chronic low dose exposure to solvents can cause functional changes in the nervous system has in recent years come from neurophysiological studies (Seppäläinen et al 1972; Seppäläinen & Tolonen 1974; Knave et al 1974, 1975). All the above studies were conducted with the aim of attempting to detect intoxication at an early stage by looking at sub-clinical manifestation.

The detection of sub-clinical manifestations, whether accomplished by analyzing performance, nerve conduction velocity, EEG or other objective measures, is viewed as particularly important for two main reasons. Firstly, these manifestations, even when reversibility is not questioned, may be indicators of undefined, non-specific functional disorders, recovery from which may be slow and tedious. Secondly, they may be early warning signs of more serious occupational disease which may develop years later.

Results of field studies

Studies 6 and 7 were restricted by the practical consideration that measurements should be accomplished without interfering with the subjects' normal work routines. Thus comprehensive and time-consuming tests had to be avoided. Interest was therefore centered on a few performance variables which could be measured in a relatively short period of time (15 min) at the beginning and at the end of a work day.

The rationale of this design is based on the underlying assumption that the effect of exposure during the day may manifest itself in an impairment of performance at the end of a work day, with return to a normal level of performance by the beginning of the following working day, i.e., after approximately 16 hours of rest from exposure. If the action of exposure lasts long enough to bridge the exposure-free period between two consecutive work days, performance should be negatively affected also at the start of a work day.

In Studies 6 and 7, measurements of performance were made principally by means of reaction time tasks. The performance variable usually analysed in reaction time tasks is the speed of performance, i.e. the reaction time proper. In the present investigations, however, performance on the tasks was also analysed with respect to measures of intraindividual variability of response. Such analysis has been advocated by a number of authors (e.g. Poulton 1965; Teichner & Olson 1971) as a means of increasing the sensitivity of the instruments with which the influence of environmental factors on human performance is studied.

No significant differences were found between anesthetic nurses and the unexposed nurses of the control group with regard to the speed of performance (Study 6). However, in a task of simple reaction time the anesthetic nurses displayed a greater irregularity of response than the unexposed nurses. This difference between the groups was observed when performance was measured in the evening at the end of a work day, but not in the morning, i.e., after about 16 hours rest from exposure. This result was interpreted as being due to an acute effect on the nervous system, caused by exposure to anesthetic gases.

A technical question could be raised as to why exposure should produce an effect on the regularity of response, while the speed of response,

i.e., the mean reaction time, apparently remained unaffected. A reasonable answer to this question could be that, in some circumstances, measurement variables associated with the variability of response in a reaction time task might reflect earlier changes of reaction pattern better than measurements of central tendency. Some support for this hypothesis is found in our study on methylene chloride (Study 5), where exposure also seems to have produced an increase in the variability of response without any concomitant change in mean reaction time. According to the above results, it seems that measurements of the variability of response can provide additional information for the analysis of performance in reaction time tasks. It should however be noted that the variability of response may be more apparent than real in cases where the level of performance is affected (Welford 1968).

Another way of analysing performance in a reaction time task is to look for systematic variation in the speed of response over time. According to Lisper & Eriksson (1973), the speed of response decreases progressively over time in tasks with high signal frequency. With such a task Lisper & Kjellberg (1972) found that the rate of deterioration in speed of performance was a better indicator of the effects of sleep deprivation than mean reaction time. Similar results were obtained in an investigation on the effects of valium (Laurell et al 1974).

In Study 7 the effects of occupational exposure to styrene were studied by means of a 10-minute reaction time task with high signal frequency (16 signal/min). Performance on the task was then analysed with respect to the speed and regularity of response as in Study 6, and with respect to the rate of decrement in performance over time in accordance with the above authors.

Highly significant differences in performance on the task were obtained between the workers exposed to styrene and the unexposed workers of the control groups. The former had longer reaction time, a greater deterioration in reaction time over time and a greater irregularity of response both at the beginning and at the end of the working day. The differences between exposed and unexposed workers appeared to be somewhat greater in the evening than in the morning. These results were interpreted as indicating that exposure to styrene had caused a functional impairment in the exposed workers' CNS. The fact that the effect was observable after about 16 hours rest from exposure, i.e., at the beginning of a work day,

seems to imply that the workers in the plastic boat industry might be subjected to an enduring biological influence. This interpretation of the nature of the performance changes observed among the workers in the plastic boat industries was also supported by the fact that a significant, though very low, positive correlation could be observed between the length of employment of the exposed workers and their deterioration in performance over time.

The investigation design adopted in Studies 6 and 7, implying measurement of performance at different times during the day, has proved to provide some information as regards the possible nature of the effects observed. Thus in Study 6 it seems possible to ascribe the observed differences in performance to an acute effect of short duration, while this interpretation seems to be excluded in Study 7.

When comparing the results from measurements of reaction time collected at different times during the day, the effects of circadian rhythms leading to shorter reaction time during the evening as compared to during the morning (Kleitman et al 1938; Hildebrand & Engel 1972) must be considered. In accordance with expectations, the mean reaction times of the control groups of both Studies 6 and 7 were lower in the evening than in the morning session. However no such tendency could be observed in the exposed groups. These results seems to imply that an effect on performance, at least on performance in reaction time tasks, need not necessarily result in manifest differences in performance before and after a day of exposure to adverse environmental factors. Since factors other than exposure or circadian rhythms can also affect performance, the use of control group seems to be necessary even in investigations where the effects are of an acute and short-lived nature.

The outcome of Studies 6 and 7 show that behavioral performance measures can be used to assess possible effects on the nervous system caused by occupational exposure to chemical agents.

In Study 6 exposure to anesthetic gases could be shown to produce only slight effects on performance. However, in this case, an effect on performance may constitute a threat not only to the well being of anesthesiologists, but also to the health care provided in the operating theatres. It therefore seems to us that even slight effects indicating a possible influence on the "vigilance" of the anesthesiologist should be given serious consideration.

In Study 7 exposure to styrene in the plastic boat industries was associated with a clear performance decrement in each of the variables analysed. The performance decrement associated with styrene could not reasonably be considered of acute, brief nature. The possibility of the effects observed being a manifestation of long lasting or even chronic intoxication should be seriously considered.

CONCLUDING REMARKS

There seem to be two major reasons for the use of behavioral methods in toxicological studies. The first reason is that behavioral measures seem to be more adequate and more sensitive in situations involving low-dose exposure than are more traditional toxicological methods. The other reason is that behavioral measures may reveal early signs of functional disorders, and thereby be useful means of preventing irreversible manifestation of intoxication. Of course, the use of behavioral methods for the first purpose would be greatly enhanced if their practical significance for the second purpose could be demonstrated.

The present investigations were conducted with the first purpose, outlined above. Thus, measurements of behavioral performance were used as indicators of functional impairment of the nervous system. It could be shown that low-dose exposure to a number of substances commonly found in working environments does exert adverse effects on the human organism. The practical significance of these findings with regard to the establishment of TLVs seems obvious, since some indications could be given concerning the concentration of certain substances which may be expected to produce functional impairment of nervous system processes.

Independent of the purpose of their use, psychological methods always rely on their capacity to provide measurements of the activity of underlying functional processes, i.e., processes on which behavior depends. In our investigations we were only concerned with the sensitivity of the methods as to their capacity to reflect behavioral processes. The use of behavioral methods as means of predicting or anticipating irreversible tissue damage, as in the second purpose outlined above, makes further demands on their validity. In order to establish the health significance

of observed behavioral changes, behavioral observations must be shown to correlate with observations reflecting different underlying processes. Such observations are found within the realm of other disciplines from which toxicology borrows its methods. Future research should therefore call for more emphasis on an interdisciplinary approach.

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